Microscopy TODAY

## Coming Events

**2010**

**Neuroscience**
November 15–18, 2010
San Diego, CA
www.sfn.org/am2010

**Eastern Analytical Symposium**
November 15–18, 2010
Somerset, NJ
www.eas.org

**MRS Fall Meeting**
November 29–December 3, 2010
Boston, MA
www.mrs.org/fall2010

**Cell Biology**
December 11–15, 2010
Philadelphia, PA
www.ascb.org/meetings

**AAFS Forensic Science**
February 21–26, 2010
Chicago, IL
www.aafs.org/aafs-2011-annual-meeting

**2011**

**TMS 2011 Annual Meeting**
February 27–March 3, 2011
San Diego, CA
www.tms.org

**PITTCON**
March 13–18, 2011
Atlanta, GA
www.pittcon.org

**FASEB Experimental Biology**
April 9–13, 2011
Washington, DC
eb@faseb.org

**MRS Spring Meeting**
April 25–29, 2011
San Francisco, CA
www.mrs.org/spring2011

**Microscopy & Microanalysis 2011**
August 7–11, 2011
Nashville, TN

**2012**

**Microscopy & Microanalysis 2012**
July 29–August 2, 2012
Phoenix, AZ

**2013**

**Microscopy & Microanalysis 2013**
August 4–8, 2013
Indianapolis, IN

**2014**

**Microscopy & Microanalysis 2014**
August 3–7, 2014
Hartford, CT

**More Meetings and Courses**
Check the complete calendar near the back of this magazine and in the MSA journal *Microscopy and Microanalysis*.



## Carmichael's Concise Review

# Localizing Channels for Learning

**Stephen W. Carmichael**
Mayo Clinic, Rochester, MN 55905

carmichael.stephen@mayo.edu

The most widely accepted model of learning at the level of the cell involves associative synaptic plasticity in brain neurons that include cortical pyramidal cells (PC). To oversimplify, for a neuron to "learn" from information coming into it, electrical events need to occur in a fairly precise pattern throughout the cell membrane.

An essential prerequisite of this model of learning at the cellular level is that input synapses that are distributed over a very large dendritic tree must be capable of sensing the precise timing of the output signal. In order to coordinate these events, it is thought that fast sodium action potentials (APs) are initiated at the axon initial segment (AIS) and propagated back through the body (soma) into the dendrites of the neuron. Physiological studies have detected voltage-gated $Na^+$ (Nav) currents in PCs and other neurons. Nav currents differ in their activation and inactivation properties, which suggests the possibility that different Nav subunits may be involved. Andrea Lorincz and Zoltan Nusser have combined immunofluorescent techniques with a very sensitive electron microscopic immunocytochemical technique to demonstrate the unequal distribution of one Nav subunit among different parts of the PC [1].

To increase the sensitivity of the immunofluorescent techniques, Lorincz and Nusser chemically fixed rat brain samples in an acidic medium, resulting in better preservation of the immunogenicity of certain receptors and ion channels. Whereas immunolabeling for Navs was stronger in the AIS and nodes of Ranvier, some signal could be detected in the dendritic tree. However, it was not possible to determine the subunit composition of the Navs or their precise localization.

To examine the subunit composition of the Navs, they used specific antibodies against different Nav subunits, including a subunit referred to as Nav 1.6. After confirming the specificity of the immunoreactions, they demonstrated the distribution of the Nav subunits in various parts of the neuron. Of particular interest was the strong signal for Nav 1.6 at the AIS and nodes of Ranvier, and also the weak signal from apical dendrites, which had no signal for the other Nav subunits.

To more precisely localize Nav 1.6 subunits on dendrites, Lorincz and Nusser used a very sensitive, quantitative electron microscopic immunogold method known as SDS-digested freeze-fracture replica-labeling (SDS-FRL). Under optimal circumstances, this method is thought to have a labeling efficiency close to 100%, which means every protein, on average, is represented by a gold particle. The spatial resolution is about 25 nm. As expected, the AISs and nodes of Ranvier were intensely labeled. Relatively low densities of gold particles could be found along dendritic shaft membranes, but not on dendritic spines (see Figure 1). After accounting for non-specific labeling, gold particles were displayed at a significantly higher density on the neuronal cell bodies, and proximal apical, proximal oblique, and distal apical dendrites. Thus, for the first time, the exceptionally high sensitivity of the SDS-FRL method revealed low, but significant, densities of the Nav 1.6 subunit in these dendritic compartments. The much higher density (about 40-fold) of labeling on AISs is consistent with earlier physiologic studies.

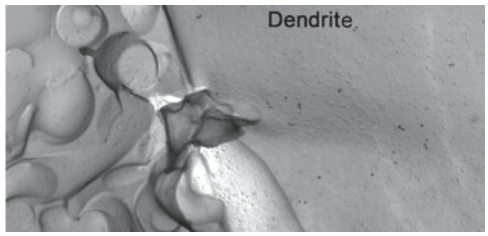


**Figure 1:** Electron micrograph of a freeze-fractured carbon-platinum replica immunolabeled for the Nav 1.6 subunit of the voltage-gated $Na^+$ channels. Small gold particles labeling the Nav 1.6 subunit are concentrated on a P-face membrane of a hippocampal pyramidal cell dendrite (right side of the image). The labeling on the P-face is consistent with the intracellular location of the epitope recognized by our antibody. Small E-face structures on the left side of the image are immunonegative.

Lorincz and Nusser have convincingly demonstrated that Nav 1.6 is the main Nav subunit in the somatodendritic compartments of PCs in the rat hippocampus. Whereas there may be other factors involved, these data support the view that the distribution of Navs, particularly the Nav 1.6 subunit, plays an important role in learning at the neuronal level [2].

## References

[1] A Lorincz and Z Nusser, *Science* 328 (2010) 906–09.
[2] The author gratefully acknowledges Dr. Zoltan Nusser for reviewing this article.



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**Carl Zeiss NTS**

One Corporation Way
Peabody, MA 01960
USA

Tel. +1978/8261500
info-usa@smt.zeiss.com
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